PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

United States Patent and Trademark Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 21 November 1997 (21.11.97)	
International application No. PCT/US97/01870	**Applicant's or agent's file reference** 21467/71
International filing date (day/month/year) 31 January 1997 (31.01.97)	**Priority date** (day/month/year) 31 January 1996 (31.01.96)
Applicant BAILEY, Steven, W. et al	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

28 August 1997 (28.08.97)

[ ] in a notice effecting later election filed with the International Bureau on:

_____

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO **34, chemin des Colombettes** **1211 Geneva 20, Switzerland**	Authorized officer S. De Michiel
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

REC'D 25 MAY 1998
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 87647.97R246	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US97/01870	International filing date *(day/month/year)* 31 JANUARY 1997	Priority date *(day/month/year)* 31 JANUARY 1996
International Patent Classification (IPC) or national classification and IPC IPC(6): A23L 1/302 and US Cl.: 426/72, 549, 801, 807,		
Applicant SOUTH ALABAMA MEDICAL SCIENCE FOUNDATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

   [✓] This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 8 sheets.

3. This report contains indications relating to the following items:

   - I [X] Basis of the report
   - II [ ] Priority
   - III [ ] Non-establishment of report with regard to novelty, inventive step or industrial applicability
   - IV [ ] Lack of unity of invention
   - V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI [ ] Certain documents cited
   - VII [ ] Certain defects in the international application
   - VIII [X] Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28 AUGUST 1997	23 APRIL 1998
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer HELEN PRATT Telephone No. (703)308-0651

Form PCT/IPEA/409 (cover sheet) (January 1994)★

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/01870

I. Basis of the report

1. This report has been drawn on the basis of *(Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments)*:

☐ the international application as originally filed.

☒ the description, pages (See Attached) , as originally filed.
pages _____ , filed with the demand.
pages _____ , filed with the letter of _____.
pages _____ , filed with the letter of _____.

☒ the claims, Nos. (See Attached) , as originally filed.
Nos. _____ , as amended under Article 19.
Nos. _____ , filed with the demand.
Nos. _____ , filed with the letter of _____.
Nos. _____ , filed with the letter of _____.

☒ the drawings, sheets/~~fig~~ (See Attached) , as originally filed.
sheets/~~fig~~ _____ , filed with the demand.
sheets/~~fig~~ _____ , filed with the letter of _____.
sheets/~~fig~~ _____ , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☒ the description, pages NONE.

☒ the claims, Nos. 4, 21-23.

☒ the drawings, sheets/~~fig~~ NONE.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/01870

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Inventive Step (IS)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Industrial Applicability (IA)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO

2. CITATIONS AND EXPLANATIONS

Claims 1, 2, 5, 9, 10, 12-20, 25-28, 31-33, 35, 36-43 lack an inventive step under PCT Article 33(3) as being obvious over Muller et al. in view of Lucas et al. and Pedersen et al.

Muller et al. disclose a composition containing 5-methyl-(6S)-tetrahydrofolic acids and 5-10 methyl-(6S)tetrahydrofolic acid. See abstract. Claims 1 and 2 differ from the reference in the use of the folate with a nutritional substance, in a particular ratio, or with a vitamin. However, Pedersen et al. disclose that it is known to use folacin in a potato flake. See col. 6, lines 1-12. Lucas et al. disclose that it is known to use folic acid in an infant food. The specification discloses that these substances are broken down in the digestive tract to the reduced form by an enzyme (col. 5, lines 9-16). If it is known that folic acid and folacin are broken down to make the claimed compositions, then it is obvious that such natural compounds can be also eaten in foods. The references after Pedersen et al. and Lucas et al. are seen to be cumulative to show an improvement in the art. Applicants admit in the specification that 5 formyl-tetrhydrofolic acid, and 5 methyl-tetrhydrofolic acid have been used in therapeutic doses. See page 5, lines 17-24. Mueller et al. disclose that invention is an improvement of 6S and ^R forms with a natural form of 6S (col. 2, lines 3-7). Certainly, it would have been obvious to use a vitamin type substance with other foods, as food enrichment is well known and vitamins are rarely taken alone except as in pills. Therefore, it would have been obvious to one of ordinary skill in the art to use a reduced folate with other food ingredients or vitamins in the claimed composition.

The further limitations as in claim 5 to a food preparation, have been discussed above. Nothing new is seen in vitamin supplementation as in claims 9,10, as it is well known to supplement enough to provide for a beneficial effect, and the use of folic acid, which is another form of folate is well known and used in foods and vitamin supplements.

Claims 12-20, 25, 26 of administering the reduced folate in (Continued on Supplemental Sheet.)

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 27-44 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph. No basis is seen in the specification for the phrase "other than a pig".

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
pages, 1-23, as originally filed.
pages, NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
numbers, NONE, as originally filed.
numbers, NONE, as amended under Article 19.
numbers, NONE, filed with the demand.
and additional amendments:
Claims 1-3, 5-20, 24-44, filed with the letter of 27 March 1998.

This report has been drawn on the basis of the drawings,
sheets, NONE, as originally filed.
sheets, NONE, filed with the demand.
and additional amendments:
NONE

V. 1. REASONED STATEMENTS:
The report as to Novelty was positive (YES) with respect to claims 1-3, 5-20, 24-44.
The report as to Novelty was negative (NO) with respect to claims NONE.
The report as to Inventive Step was positive (YES) with respect to claims 3, 6-8, 11, 24, 29, 30, 34, 44.
The report as to Inventive Step was negative (NO) with respect to claims 1-2, 5, 9-10, 12-20, 25-28, 31-33, 35-43.
The report as to Industrial Applicability was positive (YES) with respect to claims 1-3, 5-20, 24-44.
The report as to Industrial Applicability was negative (NO) with respect to claims NONE.

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
particular amounts in particular amounts in various ways have been discussed above and are obvious for those reasons as giving vitamin supplements to animals and in enteral administration is well known.

The limitations of claims new claims 27-28,31, 33, 35-43 have been discussed above except that the composition can be given to any animal except pigs. However, no basis is seen in the specification for this limitation. No reason is stated for making such a limitation. As the combined references disclose the claimed limitations, it would have been obvious to give it to various animals.

Claims 1-44 meet the requirement for industrial applicability as defined by PCT Article 33(4). The composition and methods of using reduced folates can be used for enriching the diets of various animals and humans.

Claims 3, 6, 7, 8, 11, 24, 29, 30, 34, 44 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest giving reduced folates as claimed in particular amounts to humans and some animals for nutritional supplementation.

——————— NEW CITATIONS ———————
NONE

PATENT COOPERATION TREATY

PCT

COPY

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 87647.97R246	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US97/01870	International filing date *(day/month/year)* 31 JANUARY 1997	Priority date *(day/month/year)* 31 JANUARY 1996
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   These annexes consist of a total of 8 sheets.

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3. This report contains indications relating to the following items:

   I [X] Basis of the report

   II [ ] Priority

   III [ ] Non-establishment of report with regard to novelty, inventive step or industrial applicability

   IV [ ] Lack of unity of invention

   V [X] Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

   VI [ ] Certain documents cited

   VII [ ] Certain defects in the international application

   VIII [X] Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28 AUGUST 1997	23 APRIL 1998
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer HELEN PRATT Telephone No. (703)308-0651

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/01870

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☐ the international application as originally filed.

☒ the description, pages (See Attached) , as originally filed.
pages _____ , filed with the demand.
pages _____ , filed with the letter of _____.
pages _____ , filed with the letter of _____.

☒ the claims, Nos. (See Attached) , as originally filed.
Nos. _____ , as amended under Article 19.
Nos. _____ , filed with the demand.
Nos. _____ , filed with the letter of _____.
Nos. _____ , filed with the letter of _____.

☒ the drawings, sheets/~~fig~~ (See Attached) , as originally filed.
sheets/~~fig~~ _____ , filed with the demand.
sheets/~~fig~~ _____ , filed with the letter of _____.
sheets/~~fig~~ _____ , filed with the letter of _____.

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☒ the description, pages NONE.

☒ the claims, Nos. 4, 21-23.

☒ the drawings, sheets/~~fig~~ NONE.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/01870

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
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	Claims	(Please See supplemental sheet)	NO
Industrial Applicability (IA)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO

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The further limitations as in claim 5 to a food preparation, have been discussed above. Nothing new is seen in vitamin supplementation as in claims 9,10, as it is well known to supplement enough to provide for a beneficial effect, and the use of folic acid, which is another form of folate is well known and used in foods and vitamin supplements.

Claims 12-20, 25, 26 of administering the reduced folate in (Continued on Supplemental Sheet.)

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 27-44 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph. No basis is seen in the specification for the phrase "other than a pig".

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
pages, 1-23, as originally filed.
pages, NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
numbers, NONE, as originally filed.
numbers, NONE, as amended under Article 19.
numbers, NONE, filed with the demand.
and additional amendments:
Claims 1-3, 5-20, 24-44, filed with the letter of 27 March 1998.

This report has been drawn on the basis of the drawings,
sheets, NONE, as originally filed.
sheets, NONE, filed with the demand.
and additional amendments:
NONE

V. 1. REASONED STATEMENTS:
The report as to Novelty was positive (YES) with respect to claims 1-3, 5-20, 24-44.
The report as to Novelty was negative (NO) with respect to claims NONE.
The report as to Inventive Step was positive (YES) with respect to claims 3, 6-8, 11, 24, 29, 30, 34, 44.
The report as to Inventive Step was negative (NO) with respect to claims 1-2, 5, 9-10, 12-20, 25-28, 31-33, 35-43.
The report as to Industrial Applicability was positive (YES) with respect to claims 1-3, 5-20, 24-44.
The report as to Industrial Applicability was negative (NO) with respect to claims NONE.

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
particular amounts in particular amounts in various ways have been discussed above and are obvious for those reasons as giving vitamin supplements to animals and in enteral administration is well known.

The limitations of claims new claims 27-28,31, 33, 35-43 have been discussed above except that the composition can be given to any animal except pigs. However, no basis is seen in the specification for this limitation. No reason is stated for making such a limitation. As the combined references disclose the claimed limitations, it would have been obvious to give it to various animals.

Claims 1-44 meet the requirement for industrial applicability as defined by PCT Article 33(4). The composition and methods of using reduced folates can be used for enriching the diets of various animals and humans.

Claims 3, 6, 7, 8, 11, 24, 29, 30, 34, 44 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest giving reduced folates as claimed in particular amounts to humans and some animals for nutritional supplementation.

———— NEW CITATIONS ————
NONE

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/01870

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A23L 1/302
US CL :426/72, 549, 801, 807,
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 426/72, 549, 801, 807,

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS search terms: folate, natural, isomers, leucorvin, vitamin, ascorbic acid

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,006,655 A (MULLER et al.)09 April 1991, abstract and lines 1-36	1-5
Y		6-26
X	US 3,833,739 A (PEDERSEN et al.) 03 September 1974, col. 6, lines 1-11, lines 55-65.	1-26
Y	US 1,431,525 A (HOFFMAN et al) 10 October 1922, col. 2, lines 64-80.	1-26
Y	US 2,052,219 A (DICKENS) 25 August 1936, col. 1, lines 1-9.	1

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search
21 APRIL 1997

Date of mailing of the international search report
19 MAY 1997

Name and mailing address of the ISA/US
Commissioner of Patents and Trademarks
Box PCT
Washington, D.C. 20231
Facsimile No. (703) 305-3230

Authorized officer
HELEN PRATT
Telephone No. (703)308-0651

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/01870

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4,753,926 A (LUCAS et al) 28 June 1988, col. 5, lines 15-30 and col. 6, lines 22-30.	1-26
X P	JP 408070788 A (EIICHI et al) 19 MARCH 1996, abstract.	1-26
X	JP 407147911 A (ONISHI et al.) 13 June 1995, abstract.	1-26

PCT/US 96/01878
IPEA/US 27 MAR 1998

1. A composition for human consumption comprising:

one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof;

a nutritional substance for human consumption selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof;

wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar amount, T, of said one or more natural isomers of reduced folate greater than N; and

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid.

2. A composition according to claim 1, wherein the one or more natural isomers of reduced folate is selected from the group consisting of 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, and polyglutamyl derivatives thereof.

3. A composition according to claim 1, wherein the total molar amount of said one or more natural isomers of reduced folate is between 5% and 200% of a human daily requirement for folate per customarily consumed quantity of said composition.

4. Cancelled.

5. A composition according to claim 1, wherein said nutritional substance is a food preparation.

6. The composition according to claim 5, wherein the nutritional substance is a food preparation and wherein each

gram of said food preparation further comprises no unnatural isomers of reduced folate selected from the group consisting of (6R)-tetrahydrofolic acid, 5-methyl-(6R)-tetrahydrofolic acid, 5-formyl-(6R)-tetrahydrofolic acid, 10-formyl-(6S)-tetrahydrofolic acid, 5,10-methylene-(6S)-tetrahydrofolic acid, 5,10-methenyl-(6S)-tetrahydrofolic acid, 5-formimino-(6R)-tetrahydrofolic acid, and polyglutamyl derivatives thereof, or one or more of said unnatural isomers of reduced folate in a molar amount less than T minus N.

7. A composition according to claim 5, wherein the food preparation is selected from the group consisting of breakfast foods, infant formulas, dietary supplements, complete diet formulas, and weight-loss preparations.

8. A composition according to claim 7, wherein the breakfast food is a prepared cereal, a breakfast drink mix, or a toaster pastry, and wherein the weight-loss preparations is a weight-loss drink or a weight-loss bar.

9. A composition according to claim 1, wherein the nutritional substance is an essential nutrient preparation comprising a vitamin other than ascorbic acid.

10. A composition according to claim 9, wherein the essential nutrient preparation further comprises ascorbic acid.

11. A composition according to claim 9, wherein the vitamin is present in an amount equal to or greater than 25% of the daily requirement for the vitamin per customarily consumed quantity of said essential nutrient preparation.

12. A method for increasing the folate content of a nutritional substance for human consumption comprising:

providing a nutritional substance for human consumption selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof; and

incorporating into the nutritional substance a molar amount of one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-

tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof;

wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar amount, T, of said one or more natural isomers of reduced folate greater than N; and

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid.

13. A method according to claim 12 further comprising:

incorporating into the nutritional substance a molar amount of one or more unnatural isomers of reduced folate selected from the group consisting of (6R)-tetrahydrofolic acid, 5-methyl-(6R)-tetrahydrofolic acid, 5-formyl-(6R)-tetrahydrofolic acid, 10-formyl-(6S)-tetrahydrofolic acid, 5,10-methylene-(6S)-tetrahydrofolic acid, 5,10-methenyl-(6S)-tetrahydrofolic acid, 5-formimino-(6R)-tetrahydrofolic acid, and polyglutamyl derivatives thereof, wherein the molar amount of the one or more unnatural isomers of reduced folate is less than the molar amount of the one or more natural isomers of reduced folate.

14. A method according to claim 12, wherein each of the one or more natural isomers of reduced folate is substantially chirally pure.

15. A method according to claim 12, wherein the one or more natural isomers of reduced folate is selected from the group consisting of 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, and polyglutamyl derivatives thereof.

16. A method according to claim 12, wherein the nutritional substance is an essential nutrient preparation comprising a vitamin other than ascorbic acid.

17. A method according to claim 16, wherein the essential nutient preparation further comprises ascorbic acid.

18. A method according to claim 12, wherein the nutritional substance is a food preparation and wherein said method further comprises:

incorporating a vitamin into the food preparation.

19. A method for increasing a human subject's dietary intake of folate comprising:

administering a composition according to claim 1 to the human subject.

20. A method according to claim 19, wherein said administering is carried out by enteral administration.

21. Canceled.

22. Canceled.

23. Canceled.

24. A method according to claim 19, wherein the total molar amount of said one or more natural isomers of reduced folate is between 5% and 200% of the human's daily requirement for folate per customarily consumed quantity of said composition.

25. A method according to claim 19, wherein the human is selected from the group consisting of a pregnant female; a female who has had a miscarriage; a female who has carried a fetus having a neural tube defect, a cleft lip defect, or a cleft palate defect; and a human who suffers vascular disease.

26. A method for treating a human subject afflicted with intestinal malabsorption comprising:

administering to the human subject an amount of a composition according to claim 1 effective to increase the human subject's blood folate level.

27. A composition for consumption by an animal other than a pig comprising:

one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic

acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof;

a nutritional substance for consumption by an animal other than a pig selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof;

wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar amount, T, of said one or more natural isomers of reduced folate greater than N; and

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid.

28. A composition according to claim 27, wherein the one or more natural isomers of reduced folate is selected from the group consisting of 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, and polyglutamyl derivatives thereof.

29. A composition according to claim 27, wherein the total molar amount of said one or more natural isomers of reduced folate is between 5% and 3000% of an animal daily requirement for folate per customarily consumed quantity of said composition.

30. A composition according to claim 27, wherein said nutritional substance is a food preparation.

31. The composition according to claim 30, wherein the nutritional substance is a food preparation and wherein each gram of said food preparation further comprises no unnatural isomers of reduced folate selected from the group consisting of (6R)-tetrahydrofolic acid, 5-methyl-(6R)-tetrahydrofolic

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IPEA/US 1998

acid, 5-formyl-(6R)-tetrahydrofolic acid, 10-formyl-(6S)-tetrahydrofolic acid, 5,10-methylene-(6S)-tetrahydrofolic acid, 5,10-methenyl-(6S)-tetrahydrofolic acid, 5-formimino-(6R)-tetrahydrofolic acid, and polyglutamyl derivatives thereof, or one or more of said unnatural isomers of reduced folate in a molar amount less than T minus N.

32. A composition according to claim 27, wherein the nutritional substance is an essential nutrient preparation comprising a vitamin other than ascorbic acid.

33. A composition according to claim 32, wherein the essential nutrient preparation further comprises ascorbic acid.

34. A composition according to claim 32, wherein the vitamin is present in an amount equal to or greater than 25% of the daily requirement for the vitamin per customarily consumed quantity of said essential nutrient preparation.

35. A method for increasing the folate content of a nutritional substance for consumption by an animal other than a pig comprising:

providing a nutritional substance for consumption by an animal other than a pig selected from the group consisting of a food preparation, an essential nutrient preparation, and combinations thereof; and

incorporating into the nutritional substance a molar amount of one or more natural isomers of reduced folate selected from the group consisting of (6S)-tetrahydrofolic acid, 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 10-formyl-(6R)-tetrahydrofolic acid, 5,10-methylene-(6R)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, 5-formimino-(6S)-tetrahydrofolic acid, and polyglutamyl derivatives thereof;

wherein, when the nutritional substance is a food preparation, the food preparation comprises two or more food components and each gram of said food preparation has a natural molar amount, N, of said one or more natural isomers of reduced folate, wherein N is greater or equal to zero and wherein each gram of said composition has a total molar

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MAR 1998

amount, T, of said one or more natural isomers of reduced folate greater than N; and

wherein, when the nutritional substance is an essential nutrient preparation, the essential nutrient preparation comprises a vitamin other than ascorbic acid.

36. A method according to claim 35 further comprising:

incorporating into the nutritional substance a molar amount of one or more unnatural isomers of reduced folate selected from the group consisting of (6R)-tetrahydrofolic acid, 5-methyl-(6R)-tetrahydrofolic acid, 5-formyl-(6R)-tetrahydrofolic acid, 10-formyl-(6S)-tetrahydrofolic acid, 5,10-methylene-(6S)-tetrahydrofolic acid, 5,10-methenyl-(6S)-tetrahydrofolic acid, 5-formimino-(6R)-tetrahydrofolic acid, and polyglutamyl derivatives thereof, wherein the molar amount of the one or more unnatural isomers of reduced folate is less than the molar amount of the one or more natural isomers of reduced folate.

37. A method according to claim 35, wherein each of the one or more natural isomers of reduced folate is substantially chirally pure.

38. A method according to claim 35, wherein the one or more natural isomers of reduced folate is selected from the group consisting of 5-methyl-(6S)-tetrahydrofolic acid, 5-formyl-(6S)-tetrahydrofolic acid, 5,10-methenyl-(6R)-tetrahydrofolic acid, and polyglutamyl derivatives thereof.

39. A method according to claim 35, wherein the nutritional substance is an essential nutrient preparation comprising a vitamin other than ascorbic acid.

40. A method according to claim 39, wherein the essential nutient preparation further comprises ascorbic acid.

41. A method according to claim 35, wherein the nutritional substance is a food preparation and wherein said method further comprises:

incorporating a vitamin into the food preparation.

42. A method for increasing a subject's dietary intake of folate, wherein the subject is an animal other than a pig, comprising:

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IPEA/US 27 MAR 1998

administering a composition according to claim 27 to the animal subject.

43. A method according to claim 42, wherein said administering is carried out by enteral administration.

44. A method according to claim 42, wherein the total molar amount of said one or more natural isomers of reduced folate is between 5% and 3000% of the animal's daily requirement for folate per customarily consumed quantity of said composition.

AMENDED SHEET

RECEIVED
MAY 22 1998
COPY

PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: SUSAN J. BRAMAN
JAECKLE FLEISCHMANN & MUGEL, LLP
39 STATE STREET
ROCHESTER, NEW YORK 14614-1310

PCT

NOTIFICATION OF TRANSMITTAL OF INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of Mailing *(day/month/year)* 19 MAY 1998	
Applicant's or agent's file reference 87647.97R246	IMPORTANT NOTIFICATION

International application No.	International filing date *(day/month/year)*	Priority Date *(day/month/year)*
PCT/US97/01870	31 JANUARY 1997	31 JANUARY 1996

Applicant
SOUTH ALABAMA MEDICAL SCIENCE FOUNDATION

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices)(Article 39(1))(see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

5/22/98mbr

Name and mailing address of the IPEA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	HELEN PRATT
Facsimile No. (703) 305-3230	Telephone No. (703)308-0651

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 87647.97R246	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/US97/01870	International filing date *(day/month/year)* 31 JANUARY 1997	Priority date *(day/month/year)* 31 JANUARY 1996
International Patent Classification (IPC) or national classification and IPC IPC(6): A23L 1/302 and US Cl.: 426/72, 549, 801, 807,		
Applicant SOUTH ALABAMA MEDICAL SCIENCE FOUNDATION		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets.

   ☑ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority. (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 8 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of report with regard to novelty, inventive step or industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28 AUGUST 1997	23 APRIL 1998
Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer HELEN PRATT Telephone No. (703)308-0651

Form PCT/IPEA/409 (cover sheet) (January 1994)☆

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/01870

I. Basis of the report

1. This report has been drawn on the basis of (*Substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments*):

☐ the international application as originally filed.

☒ the description, pages (See Attached) , as originally filed.
pages _____ , filed with the demand.
pages _____ , filed with the letter of _____.
pages _____ , filed with the letter of _____.

☒ the claims, Nos. (See Attached) , as originally filed.
Nos. _____ , as amended under Article 19.
Nos. _____ , filed with the demand.
Nos. _____ , filed with the letter of _____.
Nos. _____ , filed with the letter of _____.

☒ the drawings, sheets/~~fig~~ (See Attached) , as originally filed.
sheets/~~fig~~ _____ , filed with the demand.
sheets/~~fig~~ _____ , filed with the letter of _____.
sheets/~~fig~~ _____ , filed with the letter of _____.

2. The amendments have resulted in the cancellation of:

☒ the description, pages NONE.

☒ the claims, Nos. 4, 21-23.

☒ the drawings, sheets/~~fig~~ NONE.

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the ~~Supplemental Box~~ Additional observations below (Rule 70.2(c)).

4. Additional observations, if necessary:

NONE

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.
PCT/US97/01870

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. STATEMENT

Novelty (N)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Inventive Step (IS)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO
Industrial Applicability (IA)	Claims	(Please See supplemental sheet)	YES
	Claims	(Please See supplemental sheet)	NO

2. CITATIONS AND EXPLANATIONS

Claims 1, 2, 5, 9, 10, 12-20, 25-28, 31-33, 35, 36-43 lack an inventive step under PCT Article 33(3) as being obvious over Muller et al. in view of Lucas et al. and Pedersen et al.

Muller et al. disclose a composition containing 5-methyl-(6S)-tetrahydrofolic acids and 5-10 methyl-(6S)tetrahydrofolic acid. See abstract. Claims 1 and 2 differ from the reference in the use of the folate with a nutritional substance, in a particular ratio, or with a vitamin. However, Pedersen et al. disclose that it is known to use folacin in a potato flake. See col. 6, lines 1-12. Lucas et al. disclose that it is known to use folic acid in an infant food. The specification discloses that these substances are broken down in the digestive tract to the reduced form by an enzyme (col. 5, lines 9-16). If it is known that folic acid and folacin are broken down to make the claimed compositions, then it is obvious that such natural compounds can be also eaten in foods. The references after Pedersen et al. and Lucas et al. are seen to be cumulative to show an improvement in the art. Applicants admit in the specification that 5 formyl-tetrhydrofolic acid, and 5 methyl-tetrhydrofolic acid have been used in therapeutic doses. See page 5, lines 17-24. Mueller et al. disclose that invention is an improvement of 6S and ^R forms with a natural form of 6S (col. 2, lines 3-7). Certainly, it would have been obvious to use a vitamin type substance with other foods, as food enrichment is well known and vitamins are rarely taken alone except as in pills. Therefore, it would have been obvious to one of ordinary skill in the art to use a reduced folate with other food ingredients or vitamins in the claimed composition.

The further limitations as in claim 5 to a food preparation, have been discussed above. Nothing new is seen in vitamin supplementation as in claims 9,10, as it is well known to supplement enough to provide for a beneficial effect, and the use of folic acid, which is another form of folate is well known and used in foods and vitamin supplements.

Claims 12-20, 25, 26 of administering the reduced folate in (Continued on Supplemental Sheet.)

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

Claim 27-44 are objected to as lacking clarity under PCT Rule 66.2(a)(v) because practice of the claimed invention is not enabled as required under PCT Rule 5.1(a) for the reasons set forth in the immediately preceding paragraph. No basis is seen in the specification for the phrase "other than a pig".

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

I. BASIS OF REPORT:

This report has been drawn on the basis of the description,
pages, 1-23, as originally filed.
pages, NONE, filed with the demand.
and additional amendments:
NONE

This report has been drawn on the basis of the claims,
numbers, NONE, as originally filed.
numbers, NONE, as amended under Article 19.
numbers, NONE, filed with the demand.
and additional amendments:
Claims 1-3, 5-20, 24-44, filed with the letter of 27 March 1998.

This report has been drawn on the basis of the drawings,
sheets, NONE, as originally filed.
sheets, NONE, filed with the demand.
and additional amendments:
NONE

V. 1. REASONED STATEMENTS:
The report as to Novelty was positive (YES) with respect to claims 1-3, 5-20, 24-44.
The report as to Novelty was negative (NO) with respect to claims NONE.
The report as to Inventive Step was positive (YES) with respect to claims 3, 6-8, 11, 24, 29, 30, 34, 44.
The report as to Inventive Step was negative (NO) with respect to claims 1-2, 5, 9-10, 12-20, 25-28, 31-33, 35-43.
The report as to Industrial Applicability was positive (YES) with respect to claims 1-3, 5-20, 24-44.
The report as to Industrial Applicability was negative (NO) with respect to claims NONE.

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):
particular amounts in particular amounts in various ways have been discussed above and are obvious for those reasons as giving vitamin supplements to animals and in enteral administration is well known.

The limitations of claims new claims 27-28,31, 33, 35-43 have been discussed above except that the composition can be given to any animal except pigs. However, no basis is seen in the specification for this limitation. No reason is stated for making such a limitation. As the combined references disclose the claimed limitations, it would have been obvious to give it to various animals.

Claims 1-44 meet the requirement for industrial applicability as defined by PCT Article 33(4). The composition and methods of using reduced folates can be used for enriching the diets of various animals and humans.

Claims 3, 6, 7, 8, 11, 24, 29, 30, 34, 44 meet the criteria set out in PCT Article 33(2)-(4), because the prior art does not teach or fairly suggest giving reduced folates as claimed in particular amounts to humans and some animals for nutritional supplementation.

———— NEW CITATIONS ————
NONE

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 21467/71	**FOR FURTHER ACTION**	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
International application No. PCT/US97/01870	International filing date *(day/month/year)* 31 JANUARY 1997	(Earliest) Priority Date *(day/month/year)* 31 JANUARY 1996
Applicant SOUTH ALABAMA MEDICAL SCIENCE FOUNDATION		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 3 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. [ ] **Certain claims were found unsearchable** (See Box I).

2. [ ] **Unity of invention is lacking** (See Box II).

3. [ ] The international application contains disclosure of a **nucleotide and/or amino acid sequence listing** and the international search was carried out on the basis of the sequence listing
   - [ ] filed with the international application.
   - [ ] furnished by the applicant separately from the international application,
     - [ ] but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
   - [ ] transcribed by this Authority.

4. With regard to the **title**,
   - [X] the text is approved as submitted by the applicant.
   - [ ] the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,
   - [X] the text is approved as submitted by the applicant.
   - [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is:

   Figure No. _____
   - [ ] as suggested by the applicant.
   - [ ] because the applicant failed to suggest a figure.
   - [ ] because this figure better characterizes the invention.
   - [ ] None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/01870

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A23L 1/302
US CL :426/72, 549, 801, 807,
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 426/72, 549, 801, 807,

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS search terms: folate, natural, isomers, leucorvin, vitamin, ascorbic acid

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5,006,655 A (MULLER et al.)09 April 1991, abstract and lines 1-36	1-5
Y		6-26
X	US 3,833,739 A (PEDERSEN et al.) 03 September 1974, col. 6, lines 1-11, lines 55-65.	1-26
Y	US 1,431,525 A (HOFFMAN et al) 10 October 1922, col. 2, lines 64-80.	1-26
Y	US 2,052,219 A (DICKENS) 25 August 1936, col. 1, lines 1-9.	1

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
21 APRIL 1997	19 MAY 1997

Name and mailing address of the ISA/US	Authorized officer
Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	HELEN PRATT
Facsimile No. (703) 305-3230	Telephone No. (703)308-0651

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US97/01870

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 4,753,926 A (LUCAS et al) 28 June 1988, col. 5, lines 15-30 and col. 6, lines 22-30.	1-26
X P	JP 408070788 A (EIICHI et al) 19 MARCH 1996, abstract.	1-26
X	JP 407147911 A (ONISHI et al.) 13 June 1995, abstract.	1-26

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF RECEIPT OF RECORD COPY

(PCT Rule 24.2(a))

To:

BRAMAN, Susan, J.
Nixon, Hargrave, Devans & Doyle
L.L.P.
Clinton Square
P.O. Box 1051
Rochester, NY 14603
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)	**IMPORTANT NOTIFICATION**
19 March 1997 (19.03.97)	
Applicant's or agent's file reference	**International application No.**
21467/71	PCT/US97/01870

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

Name(s) of the applicant(s) and State(s) for which they are applicants:

SOUTH ALABAMA MEDICAL SCIENCE FOUNDATION (for all designated States except US)
BAILEY, Steven, W. et al (for US)

International filing date	:	31 January 1997 (31.01.97)
Priority date(s) claimed	:	31 January 1996 (31.01.96)
Date of receipt of the record copy by the International Bureau	:	18 March 1997 (18.03.97)
List of designated Offices	:	

EP :AT,BE,CH,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE
National :AU,CA,CN,JP,US

ATTENTION

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

- [X] time limits for entry into the national phase;
- [X] confirmation of precautionary designations;
- [ ] requirements regarding priority documents.

A copy of this Notification is being sent to the receiving Office and to the International Searching Authority.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer:
Eugénia Santos

Telephone No. (41-22) 730.91.11

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF RECEIPT OF RECORD COPY

(PCT Rule 24.2(a))

To:

BRAMAN, Susan, J.
Nixon, Hargrave, Devans & Doyle
L.L.P.
Clinton Square
P.O. Box 1051
Rochester, NY 14603
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)	**IMPORTANT NOTIFICATION**
19 March 1997 (19.03.97)	
Applicant's or agent's file reference	**International application No.**
21467/71	PCT/US97/01870

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

Name(s) of the applicant(s) and State(s) for which they are applicants:

SOUTH ALABAMA MEDICAL SCIENCE FOUNDATION (for all designated States except US)
BAILEY, Steven, W. et al (for US)

International filing date	:	31 January 1997 (31.01.97)
Priority date(s) claimed	:	31 January 1996 (31.01.96)
Date of receipt of the record copy by the International Bureau	:	18 March 1997 (18.03.97)
List of designated Offices	:	

EP :AT,BE,CH,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE
National :AU,CA,CN,JP,US

ATTENTION

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

- [X] time limits for entry into the national phase;
- [X] confirmation of precautionary designations;
- [ ] requirements regarding priority documents.

A copy of this Notification is being sent to the receiving Office and to the International Searching Authority.

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer:
Eugénia Santos

Telephone No. (41-22) 730.91.11

Copy for the designated Office (DO[redacted])

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

BRAMAN, Susan, J.
Jaeckle Fleischmann & Mugel, LLP
39 State Street
Rochester, NY 14614-1310
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)
04 August 1997 (04.08.97)

Applicant's or agent's file reference
21467/71

IMPORTANT NOTIFICATION

International application No.
PCT/US97/01870

International filing date (day/month/year)
31 January 1997 (31.01.97)

1. The following indications appeared on record concerning:

[ ] the applicant [ ] the inventor [X] the agent [ ] the common representative

Name and Address
BRAMAN, Susan, J.
Nixon, Hargrave, Devans & Doyle LLP
Clinton Square
P.O. Box 1051
Rochester, NY 14603
US

State of Nationality

State of Residence

Telephone No.

Facsimile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

[ ] the person [ ] the name [X] the address [ ] the nationality [ ] the residence

Name and Address
BRAMAN, Susan, J.
Jaeckle Fleischmann & Mugel, LLP
39 State Street
Rochester, NY 14614-1310
US

State of Nationality

State of Residence

Telephone No.
716 262 3640

Facsimile No.
716 262 4133

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

[X] the receiving Office
[ ] the International Searching Authority
[ ] the International Preliminary Examining Authority
[X] the designated Offices concerned
[ ] the elected Offices concerned
[ ] other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
Eugénia Santos

Telephone No.: (41-22) 338.83.38

Form PCT/IB/306 (March 1994)

001622851

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF THE RECORDING OF A CHANGE

(PCT Rule 92bis.1 and Administrative Instructions, Section 422)

To:

BRAMAN, Susan, J.
Jaeckle Fleischmann & Mugel, LLP
39 State Street
Rochester, NY 14614-1310
ETATS-UNIS D'AMERIQUE

Date of mailing (day/month/year)
04 August 1997 (04.08.97)

Applicant's or agent's file reference
21467/71

IMPORTANT NOTIFICATION

International application No.
PCT/US97/01870

International filing date (day/month/year)
31 January 1997 (31.01.97)

1. The following indications appeared on record concerning:

☐ the applicant ☐ the inventor ☒ the agent ☐ the common representative

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2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

☐ the person ☐ the name ☒ the address ☐ the nationality ☐ the residence

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3. Further observations, if necessary:

4. A copy of this notification has been sent to:

☒ the receiving Office
☐ the International Searching Authority
☐ the International Preliminary Examining Authority
☒ the designated Offices concerned
☐ the elected Offices concerned
☐ other:

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer
Eugénia Santos

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PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION CONCERNING
AMENDMENTS OF THE CLAIMS

(PCT Rule 62 and
Administrative Instructions, Section 417)

To:

United States Patent and Trademark
Office
(Box PCT)
Crystal Plaza 2
Washington, DC 20231
ETATS-UNIS D'AMERIQUE

in its capacity as International Preliminary Examining Authority

Date of mailing:	
21 November 1997 (21.11.97)	
International application No.: PCT/US97/01870	International filing date: 31 January 1997 (31.01.97)
Applicant: SOUTH ALABAMA MEDICAL SCIENCE FOUNDATION et al	

The International Bureau hereby informs the International Preliminary Examining Authority that no amendments under Article 19 have been received by the International Bureau (Administrative Instructions, Section 417)

The International Bureau of WIPO
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